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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SZPERKA, MICHAEL EDWARD	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 09/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/001,938	ALBANI ET AL.	
	Examiner	Art Unit	
	Michael Szperka	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-60 and 62-74* is/are pending in the application.

4a) Of the above claim(s) *1-56,60 and 67-73* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *57-59, 62-66, and 74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed June 14, 2004 is acknowledged.

Claim 61 has been cancelled.

Claim 74 has been added.

Claims 57-59, 62, and 64-66 have been amended.

Claims 1-60 and 62-74 are pending.

2. Applicant's election with traverse of Group III (claims 57-60, 62-66, and 74) and the bacterial dnaJ peptide species of SEQ ID No. 3 in the reply filed on June 14, 2004 is acknowledged. Because Applicant did not distinctly and specifically point out the supposed errors in the grouping of claims in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). The traversal of the species election is on the grounds that each of the peptides set forth in the claims share a commonality of operation, function and effect. This is not found persuasive because these peptides do not share a commonality of structure. The requirement is still deemed proper and is therefore made FINAL.

3. Claims 1-56, 60, and 67-73 are withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

4. Claims 57-59, 62-66, and 74 are under examination as they read on the bacterial dnaJ sequence comprising SEQ ID NO: 3.

5. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. However, the provisional application upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims 57-60, 62-66, and 74 of this application.

The sequence of the elected dnaJ peptide species, SEQ ID NO: 3 (QKRAAYDQYGHAAFEQ) is not present in U.S. provisional application 60/245,181, filed November 1, 2000. Therefore, the priority date for the elected claims (claims 57-59, 62-66 and 74) is deemed to be that of the instant application, USSN 10/001,938, filed on October 31, 2001.

6. Applicant's IDS forms, filed 08/04/03 and 10/10/03, are acknowledged. Applicant's reference BQ in the 10/10/03 IDS has been crossed out, as it is incomplete due to the lack of a date for the GenCore Accession number.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 57-59, 62-66, and 74 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the peptide consisting of SEQ ID NO: 3 and compositions that contain said peptide, does not reasonably provide enablement for peptides and compositions that **comprise** SEQ ID NO: 3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The specification contains guidance for making the peptide of SEQ ID NO: 3, but it does not provide guidance for how to make **any** peptide that **comprises** SEQ ID NO: 3 that maintains the disclosed utility of inducing pro-inflammatory cytokine and proliferative responses in cells isolated from patients diagnosed with oligoarticular juvenile idiopathic arthritis (oJIA) (see particularly Example 3, Table 1, and Figure 3). The instant specification discloses in paragraph 8 that "the immunogenic peptide can be **any** immunogenic portion of the dnaJ hsp..." and then identifies specific sequences that are immunogenic for use in the instant invention. The term comprising is open, allowing any number of residues to be added to either end of the specified sequence, but the specification appears to be silent as to what additions can be made without altering the functional activity of the peptide, other than the disclosure that the full-length bacterial dnaJ protein is immunogenic and induces proliferative responses in PBMC from oJIA patients in Example 1. Additionally, Applicant has recited a chimeric polypeptide comprising SEQ ID NO: 3 in claim 58, and discloses in paragraph 56 of the instant

specification that the components are 'joined together such that the functions of the linked peptides is maintained, and such that the chimeric polypeptide exhibits the functions of each component peptide." A reasonable correlation must exist between the scope of the claims and the scope of the enablement set forth. Without sufficient guidance, a person of skill in the art would not know what additions are consistent with maintenance of the peptide's utility and immunogenicity without further experimentation, especially when these additions are derived from heterologous sources that have their own activity that also must be maintained.

> Immunogenicity is not an intrinsic property of a macromolecule but rather is a condition dependent on a number of interrelated factors involved in the total biological system. For example, immunogenicity is determined, in part, by four properties of the immunogen: its foreignness, molecule weight, chemical composition and complexity and ability to be degraded by antigen presenting cell enzymes. In addition, the development of an immune response will depend on certain properties of the biological system that the antigen encounters. (Immunology, Kuby, page 74 in particular, 1992.)

The ability of an immunogen to be degraded and ultimately presented in an antigen processing cell is potentially the most unpredictable of these events, as evidenced by the failure to detect some epitopes of the model antigen OVA after it has been fused to various other sequences (Fernandes et al., Eur. J. Immunol. 2000, 30: 2333-2343, see entire document, abstract in particular). Due to the unpredictability concerning the maintenance of functional utility and immunogenicity in cases other than those consisting of SEQ ID NO: 3 and the limited guidance of the specification, such experimentation is unnecessarily, and improperly, extensive and undue.

9. This is a rejection under 35 USC § 112, first paragraph, "written description" (and not new matter).

Claims 57-59, 62-66, and 74 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time the application was filed.

The specification provides written description for a peptide consisting of SEQ ID NO: 3, but there is insufficient written description to encompass "a peptide **comprising** SEQ ID NO: 3" because the relevant identifying characteristics such as structure or other physical and/or chemical characteristics of "a peptide **comprising** SEQ ID NO: 3" encompassed by the claimed invention are not set forth in the specification as filed.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

Paragraphs 8 and 9 of the instant specification list dnaJ peptides from human and bacterial sources and indicate that they are immunogenic and can modulate an immune response by increasing or decreasing an inflammatory response associated with the immune response. Paragraph 8 indicates that the immunogenic peptide can be any immunogenic portion of the dnaJ hsp. As such, it appears that Applicant is relying

on functional attributes (immunogenicity and immune response modulation) rather than a structural attribute to describe the broad genus of molecules encompassed by a "peptide **comprising** SEQ ID NO: 3". The specification does not provide for the correlation between the chemical structure and the function of the genus "peptides **comprising** SEQ ID NO: 3" currently encompassed by the claimed invention. The reliance on the disclosed limited example of a peptide consisting of SEQ ID NO: 3 does not provide sufficient support for the written description of any "peptide **comprising** SEQ ID NO: 3" that retains the disclosed utility of inducing pro-inflammatory cytokine and proliferative responses in cells isolated from patients diagnosed with oligoarticular juvenile idiopathic arthritis (oJIA) (see particularly Example 3, Table 1, and Figure 3).

The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, § 1 "Written Description" Requirement make clear that if a claimed genus does not show actual reduction to practice for a representative number of species, then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3).

In the absence of structural characteristics that are shared by the sequences that may be added to a sequence consisting of SEQ ID NO: 3, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus of sequences comprising SEQ ID NO: 3. Thus, Applicant was not in possession of the claimed genus. See University of California v. Eli Lilly and Co. 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997).

"Adequate written description requires a precise definition, such as by structure, formula, chemical name or physical properties, not a mere wish or plan for obtaining the claimed chemical invention." Id. at 1566, 43 USPQ2d at 1404 (quoting Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606). Also see Enzo-Biochem v. Gen-Probe 01-1230 (CAFC 2002).

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claim 74 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "immune response-modulating" is not clearly defined in the specification, and modulating encompasses the mutually exclusive properties of either increasing or decreasing an immune response. Therefore, a person of ordinary skill in the art would not be apprised of the metes and bound of the composition in the invention as claimed.

Applicant is reminded that any amendment to the claims to obviate a rejection must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 57-59, 62-66 and 74 are rejected under 35 U.S.C. 102(b) as being anticipated by Carson et al., U.S. Patent No. 5,773,570 (see entire document).

Carson et al. teach a purified antigenic *Escherichia coli* dnaJ protein that comprises SEQ ID NO: 3 and its use in a vaccine (column 2, lines 33-36, column 4, lines 52-54 and 62-67, and column 5, lines 1-4 and 13-16 in particular). Also disclosed are fusion proteins containing dnaJ (column 11, lines 22-31 and column 15, Example 1 in particular) that can be included in a pharmaceutical composition. Such compositions can include immunoadjuvants (paragraph spanning columns 5 and 6 in particular), such as Freund's complete or incomplete adjuvant (column 11, lines 38-41 in particular) or cytokines. Cytokines disclosed as particularly useful in the invention are the pro-inflammatory cytokine IL-6 (column 6, lines 2-5 in particular) and the anti-inflammatory cytokine TGF-β (column 6, lines 24-32 in particular).

The teachings of the prior art anticipate the claimed invention.

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Szperka whose telephone number is 571-272-2934. The examiner can normally be reached on M-F 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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